# University of California, San Diego Winter 2021
# CHEM 165/265, BIMM162, BGGN262: Three-Dimensional Electron Microscopy

**Professor:**

Dr. Mark Herzik
Natural Sciences Building 4105
email: mherzik<at>ucsd.edu (or use the email within Canvas)

**Course Lectures:**

All lectures will be held remotely via Zoom during the regularly scheduled class time slot. Lecture slides will be uploaded to Canvas prior to the scheduled date/time listed on the syllabus. All lecture recordings will be made available on Canvas within 24 hours post lecture.

The zoom link for the lecture will be posted within Canvas. Please check Canvas for Zoom information to ensure you have the most up-to-date link.

| | | |
|---|---|---|
| Monday/Wednesday | 9:30 – 10:50 a.m. (PST) | Remote via Zoom |

**Lecture Participation:**

Participation in this class is required. A lot of material will be covered during this course and concepts introduced early on in the course will serve as a foundation for later topics. It is imperative that a full understanding of the material is obtained and asking questions is the best way to ensure this happens.

For each lecture, 1-2 people will be assigned a "moderator" role. The moderators will help Dr. Herzik ensure questions posed in the Zoom Chat window are answered and allow for participants to ask questions during the live lecture.

**Office Hours:**

| | | |
|---|---|---|
| Friday | 9:00 – 9:50 a.m. (PST) | Remote via Zoom |

The Zoom link for office hours will be posted within Canvas. Please check Canvas for Zoom information to ensure you have the most up-to-date link.

Additional office hours can be scheduled by appointment if necessary
***please email first to schedule appointments***

**Course Web Page**

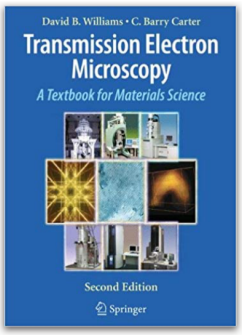
https://canvas.ucsd.edu (log in and choose CHEM165_WI21_A00).

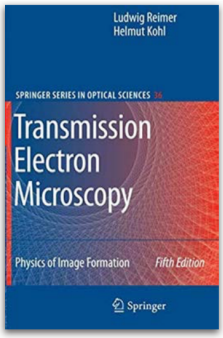
*Access to the class website is required. If you are auditing the class, please contact Dr. Herzik to obtain access.*

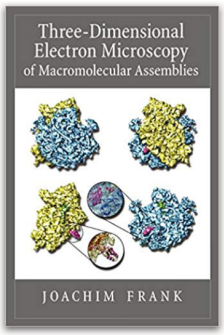
**Textbook:**

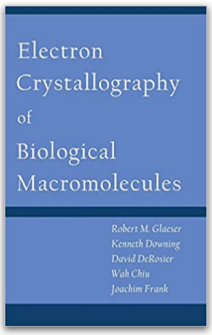
The field of cryogenic electron microscopy (Cryo-EM) is fast-evolving. As such, there is no single textbook that covers all of the relevant topics and the latest advances. The course website contains a collection of materials and links to external material that are considered to be useful to learning cryo-EM.

Here is a list of textbooks that cover various aspects of EM in great detail, each with a slightly different emphasis:




NOTE: you are not required to purchase these textbooks for this course, but they may be very relevant if cryo-EM is a critical aspect of your thesis/research/career/hobby.

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**Additional Materials:**

Professor Tim Baker (UCSD Chemistry and Biochemistry) previously taught this course from 2007 to 2013 and has assembled a wonderful set of notes. These supplementary materials, as well supplementary websites will be posted on the course Canvas site.

*The lecture slides, Prof. Baker's lecture notes, as well as assigned additional reading will be required for successful completion of this course as it is impossible to cover all necessary materials in adequate depth during lectures.*

**Homework:**

This course covers a lot of different concepts and requires you to both understand them and apply them. To help achieve this, **three** separate homework assignments will be posted on the Canvas class website that contains questions referencing material covered in class and will often mimic those given on the exams. Each assigned homework will be submitted for a grade.

https://canvas.ucsd.edu (The online homework can be accessed through Canvas. See the section on Online Homework below.)

**Group Presentations:**

6 groups of students will be required to pick a paper from the list of papers provided by Dr. Herzik and give a 25-minute group presentation on the topics covered in the paper. The scope of the presentation and the list of papers will be provided on Canvas.

Each paper will be available to be presented by one group only, on a first-come-first-serve basis.

NOTE: the paper that is to be presented cannot be the same paper that the student submits the written critique for.

Each person in the audience will submit an anonymous evaluation of the presenters that will be considered by Dr. Herzik in the final group presentation score.

**Paper Critique:**

Each student will be required to pick a paper from the list of papers provided by Dr. Herzik and provide a two-page written critique. The scope of the critique and the list of papers will be available on Canvas. Each paper will only be available to be critiqued by 2-3 people on a first-come-first-serve basis.

**Discussion Board:**

Canvas has a built-in Discussion Board that can and should be used to pose questions and discuss the materials presented in class. More than likely, if you happen to have a question about the material then others in the class do as well and it warrants further clarification and discussion.

NOTE: this is not Reddit and everyone is expected to behave in a respectful and cordial manner in accordance with UCSD's Principle of Community policies (https://ucsd.edu/about/principles.html). If someone is behaving inappropriately, they will be reprimanded in accordance with UCSD's policies.

**Special Accommodations:**

If you have been given an Authorization for Accommodation (AFA) letter from the Office of Students with Disabilities (OSD), you must provide the instructor and the OSD Liaison (for Chemistry contact chemosd@ucsd.edu, for Biology contact bioosd@ucsd.edu) with a copy of the letter before any accommodations will be provided. All exam scheduling will be coordinated by you and the instructor, with involvement from the OSD Liaison as needed. In order to guarantee accommodations, you must follow the guidelines established by the Instructor and/or Liaison. OSD exams will run concurrently with the scheduled exam.

**Special Circumstances:**

You must communicate special needs, including those based on medical conditions or religious beliefs, prior to January 22nd. These needs will be taken into account only after they have been discussed with Dr. Herzik.

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## CATALOG DESCRIPTION

*CHEM165/CHEM265/BIMM162/BGGN262:* Three-Dimensional (3D) Electron Microscopy of Macromolecules. The resolution revolution in cryo-electron microscopy has made this a key technology for the high-resolution determination of structures of macromolecular complexes, organelles, and cells. The basic principles of transmission electron microscopy, modern cryo-electron microscopy, image acquisition, and 3D reconstruction will be discussed. Examples from the research literature using this state-of-the-art technology will also be discussed. May be co-scheduled with BIMM 162/CHEM 165. Students may not receive credit for BGGN 262 and CHEM 265. (4 credits).

## COURSE OBJECTIVES

Upon completion of this course, you *should* be able to:

1. explain why electrons are used to image specimens and how these electrons interact with the specimens
2. describe the design of a transmission electron microscope, explain the function of each lens and lens type, and describe how electron microscopes both generate and manipulate electrons
3. understand how images are formed in the electron microscope, the physics behind contrast and image formation, and how these electrons are recorded using cameras
4. explain techniques used to prepare biological specimens for analysis by electron microscopy, describe common pitfalls and methods to overcome these pitfalls, and the challenges associated with preparing and imaging biological specimens by electron microscopy
5. explain why Fourier Transforms are necessary for electron microscopy, how and where they manifest during imaging, and how two-dimensional images are utilized to generate three-dimensional volumes
6. explain the processes of image analysis, image curation, particle picking, two-dimensional and three-dimensional classification and refinement strategies, and analysis
7. explain why validation is necessary in electron microscopy and describe the methods available to evaluate and validate images, volumes, atomic models, etc.
8. describe the differences in sample preparation, imaging, and analysis of the various electron microscopy modalities
9. understand the capabilities, limitations, and applications of the different electron microscopy techniques and describe their strengths and pitfalls

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**Tentative Course Schedule***

| Date | | Day | Lecture Number | Lecture Topic(s) | Breakout Topic |
|---|---|---|---|---|---|
| January | 4 | M | 1 | Course Introduction | Introductions |
| | 6 | W | 2 | Basics of cryo-EM | Chimera tutorial 1 |
| | 11 | M | 3 | Design of the TEM | Chimera tutorial 2 |
| | 13 | W | 4 | Image formation | CTF tutorial |
| | ***18*** | ***M*** | ***No class UCSD Holiday*** | | |
| | 20 | W | 5 | Sample preparation & challenges | Facility tour – Sample Prep |
| | | | Homework #1 due at 11:55 pm (PST) | | |
| | 25 | M | 6 | Radiation damage | Facility tour – Microscopes |
| | 27 | W | 7 | Cameras & imaging conditions | |
| February | **1** | **M** | **Exam 1 (Lectures 2-7)** | | |
| | 3 | W | 8 | Automated Data Collection | Facility tour – Data Collection |
| | 8 | M | 9 | Historical perspective & Fourier Analysis | |
| | 10 | W | 10 | 2D Image analysis & 3D Reconstruction | cryoSPARC tutorial 1 |
| | | | Homework #2 due at 11:55 pm (PST) | | |
| | ***15*** | ***M*** | ***No class UCSD Holiday*** | | |
| | 17 | W | 11 | 3D Refinement & Classification | cryoSPARC tutorial 2 |
| | **22** | **M** | **Exam 2 (Lectures 8-11)** | | |
| | 24 | W | 12 | Model Building & validation | COOT tutorial 1 |
| March | 1 | M | 13 | Tomography data acquisition & reconstruction | COOT tutorial 2 |
| | 3 | W | 14 | Tomography data mining & subtomograms | Facility tour – FIB |
| | | | Homework #3 due at 11:55 pm (PST) | | |
| | 8 | M | Group Presentations | | |
| | 10 | W | Group Presentations | | |
| | **12** | **F** | **Written critique Due** | | |
| | **17** | **W** | **Final Exam (Lectures 12-14 & Cumulative)** | | |

***The course schedule is subject to change to accommodate the needs and demands of the class.**

****Exam I is Wednesday, February 1st from 9:30 am – 10:50 pm (PST) via Canvas.**

****Exam II is Wednesday, February 22nd from 9:30 pm – 10:50 pm (PST) via Canvas.**

****Final Exam is Wednesday, March 17th from 8:00 – 11:59 am (PST) via Canvas.**

*****Written paper critique is due Wednesday, March 17th 11:50 am (PST) via Canvas.**

## NOTES ON INSTRUCTION

As per UCSD's decision in response to COVID-19, all instruction in Winter 2021, including lectures, office hours and discussion sections, will be delivered remotely. Please check your Canvas page frequently for updates and instructions. If you are in need of a laptop, please email Vice Chancellor – Student Affairs vcsa@ucsd.edu to rent one.

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I will record all lectures and post them on Canvas in following each lecture. These lectures will be held in the originally scheduled class time (Monday/Wednesday, 9:30 – 10:50 am (PST)). There will be a Q&A session each Monday 12:00-12:50 for you to talk to me about course material (check Canvas for the Zoom link to connect to me in Zoom).

This syllabus and course schedule are subject to change to adjust to the dynamic situation on campus. Check for updates at https://coronavirus.ucsd.edu/

All student-teacher or student-student interactions *MAY or WILL be recorded for rebroadcast at another time.* What this means is the following: that video and audio for these sessions will possibly be in the Public Domain, meaning others will be able to see them (a)synchronously and as a result your audio and video interactions with the Instructor or other students. Additionally, we cannot guarantee that any other participant involved in the session is not recording it without our knowledge.

**LECTURE**

The viewing of all lectures is essential and expected. You are responsible for all announcements and concepts covered in lecture. During lecture I will present concepts, show animations/movie clips, and provide an opportunity for you to begin to practice new skills. To get the most out of lecture, please read the suggested pages and suggested videos before attending the corresponding lecture. "Skeleton" lecture notes will be available on our Canvas course site prior to each lecture. I would recommend using these skeleton slides while viewing the recorded lectures so that, during these lectures, you can take detailed notes on your outlines. Study tip: after lecture, read the text again along with your completed notes, and work the relevant end of chapter problems. The lecture schedule above, with the exception of exam dates, is subject to change.

**ONLINE HOMEWORK**

During the quarter, you will complete three online homework assignments. The dates on which these assignments are due are listed in this syllabus. You will have access to each homework assignment until the day after the homework is due. Adjustments to the due dates may be made to account for fluctuations in the course schedule.

**EMAIL ETIQUTTE**

Before e-mailing the instructor, please consider carefully whether your question might be already answered in the syllabus, or whether it is best to ask your question in person during office hours, or whether the question(s) are better suited for the Discussion Board (see above). For example, it is difficult to e-mail about concepts in Fourier analysis or that require drawings or demos. If you send an e-mail, make sure to **include BIMM 162, BGGN 262, CHEM 165, or CHEM 265 in the subject header**. You must send your email from your UCSD address; please make it clear who you are. As always, a well-written and professional e-mail greatly increases the likelihood that you will get a response in a timely manner.

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## COURSE GRADES

There will be two exams, three online homework assignments, a group presentation, a written paper critique, and a final exam for this course. The point breakdown is as follows:

| | |
|---|---|
| Exam I[1*] | 50 |
| Exam II[1*] | 50 |
| Final Exam[1] | 100 |
| Online Homework[2] | 150 |
| Group Presentation[3] | 50 |
| Presentation assignments[4] | 50 |
| Written paper critique[5] | 50 |
| **Total points** | **500 points possible** |

The course grade will be based on the following scale**:

| % | 100 | 99-94 | 93-92 | 91-90 | 89-82 | 81-80 | 79-78 | 77-70 | 69-68 | 67-60 | 59-0 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Grade | A+ | A | A– | B+ | B | B– | C+ | C | C– | D | F |

**Although I will never raise the grading scale, I reserve the right to lower it at the end of the semester.)

1. *Exams:* Two midterms and one final exam will be given during the quarter. Because the course content builds during the semester, you can expect the second exam to be somewhat cumulative in nature. The final exam will be mostly cumulative with some focus on the later lectures not covered by exam 2. **There are no make-up exams**.
    a. Each exam will comprise a mixture of True/False, multiple-choice, and fill-in-the-blank that will be accessed via Canvas using the built-in exam resources. For each exam, several short answer questions will require hand-written responses to be uploaded via Gradescope/Canvas prior to the end of the scheduled exam window. We will work with you to ensure you are comfortable with this exam style, but I would recommend becoming familiar with each aspect prior to the exam date.
    b. Once graded and returned, any questions pertaining to the content or grading of the midterms must be resolved with Dr. Herzik (preferably during office hours). Students will have until the final day of class to resolve any issues pertaining to the midterm exams. No corrections may be submitted for the final exam.

2. *Online Homework:* Each unit covered in this course will have an associated homework assignment to be completed through Canvas. Each assignment will be worth 50 points. All assignments will be due by 11:55 pm (PST) on the date indicated on the assignment. There will be a 50% penalty for any homework submitted after the due date (*unless written permission has been obtained by Dr. Herzik*).

3. *Group Presentations:* 4-6 groups of students will be required to pick a paper from the list of papers provided by Dr. Herzik on the Canvas course web site. Each group will give a 25-minute presentation that details the scope of the paper, the techniques used, the conclusion(s) from the paper, and potential follow-up studies. Each student will be required to contribute to the evaluation of the paper, the building of the presentation slides, as well as presenting the paper to the class. Each member of the group will rate the contribution of the other members.

4. *Presentation Assignment:* Each group of presenters will provide 5 questions relevant to the paper being presented for members of the audience to complete. The scope and range of questions will be generated in collaboration with Dr. Herzik. Each assignment will be available in Canvas. Each student will also rate the effectiveness of the group presentation that will later be used in assigning grades for the group members.

5. *Written Paper Critique:* Each student will be required to pick a paper from the list of papers provided by Dr. Herzik on the Canvas course web site. The scope of the written critique will be available on Canvas.

* *Special Circumstances:* An alternate exam may be administered prior to the scheduled time *only* in cases where travel for a university sanctioned business or function, which cannot be rescheduled, interferes with an exam date. *If such plans do interfere with an exam date, then it is your responsibility to schedule an alternate exam date prior to the scheduled date. This alternate date must be*

*finalized at least two weeks prior to the scheduled exam date.* You must show proper documentation from the appropriate university official for an early exam to be administered.

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**HOW TO SUCCEED IN 3DEM of Macromolecules**

Success is a matter of exposure and practice. The following are some tips for success:

- Attend and participate fully in **ALL** lectures.

- **PLEASE KEEP UP** with the concepts being presented. I would recommend you do a little studying daily or a few times a week. **Do not put off your studying until the test.** Try rewriting your notes as if you were going to explain each day's concepts to someone who was not able to attend class. Look over the learning objectives. Create your own study guides and practice exam questions (and then try out those questions on one of your peers!). Biochemistry is a fascinating subject, but it's also very dense. There is a lot to learn, and you will need to keep up in order to succeed. You must also understand that **THIS COURSE IS CUMULATIVE**! The concepts we learn this week will build on those that we covered last week. If you didn't "get it" the first time, you do not have the luxury of saying, "I don't like this stuff. I can't learn it, so I'll do bad on this test and better on the next one." EM does not work that way! If you don't understand the concepts we are learning now, you will have continued difficulty with the concepts we will learn in the future. If you get stuck, get help sooner rather than later. I would strongly recommend you attend Office Hours each week and/or contact Dr. Herzik outside of class for assistance.

- Homework questions can provide you with a lot of practice if you approach them correctly. Do your homework problems as if you were taking a test. Try to answer them without outside help. This will allow you to identify problem areas.

- Study with others outside of class. If you are able to coherently explain a concept or idea to someone else, you can be confident that you understand the material.

- When you study for exams, look over your lecture notes, the learning objectives, and online homework/quiz questions. Create your own study guides and exam questions for practice. Use your own exam questions to quiz someone else (and have them quiz you with the exam questions that they made up). Personally, I found that the best way for me to study for my classes was to (1) rewrite my class notes each day in a lot of detail—as if I had to teach a class about the material we covered that day, (2) create a study guide and write some potential exam questions, and (3) quiz a friend about course material several times before the test (and have them quiz me). **Keep in mind that I will be asking you to not only recall the information we have discussed in class, but to apply it to new situations on your exams. Don't be satisfied with simply memorizing the information from class!**

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**UC SAN DIEGO POLICY ON INTEGRITY OF SCHOLARSHIP (*excerpted*)**

Integrity of scholarship is essential for an academic community. The University expects that both faculty and students will honor this principle and in so doing protect the validity of University intellectual work. For students, this means that all academic work will be done by the individual to whom it is assigned, without unauthorized aid of any kind. Instructors, for their part, will exercise care in planning and supervising academic work, so that honest effort will be upheld.

**Instructors' Responsibility**

The Instructor shall state in writing how graded assignments and exams will contribute to the final grade in the course. If there are any course-specific rules required by the Instructor for maintaining academic integrity, the instructor shall also inform students of these in writing.

**Students' Responsibility**

Students are expected to complete the course in compliance with the instructor's standards. No student shall engage in an activity that involves attempting to receive a grade by means other than honest effort; for example:

- No student shall knowingly procure, provide, or accept any unauthorized material that contains questions or answers to any examination or assignment that is being, or will be, administered.
- No student shall complete, in part or in total, any examination or assignment for another person.
- No student shall knowingly allow any examination or assignment to be completed, in part or in whole, for himself or herself by another person.
- No student shall plagiarize or copy the work of another person and submit it as his or her own work. No student shall employ aids excluded by the instructor in undertaking course work or in completing any exam or assignment.
- No student shall alter graded class assignments or examinations and then resubmit them for regrading.
- No student shall submit substantially the same material in more than one course without prior authorization.

For the full UCSD policy, visit http://senate.ucsd.edu/Operating-Procedures/Senate-Manual/appendices/2. For additional information, visit the Academic Integrity Office (https://students.ucsd.edu/academics/academic-integrity/index.html).